

WHAT IS CLAIMED IS:

1. A method for increasing or decreasing drug resistance in a target bacteria, yeast, plant or mammalian cell comprising altering the ATP gradient across the biological membrane of the target cell.

2. A method for altering the ATP gradient across the biological membrane of a target bacteria, yeast, plant or mammalian cell to achieve an increase in drug resistance comprising up-regulating an ecto-phosphatase in the target cell.

3. The method of claim 2 further comprising up-regulating an ABC transporter in the target cell.

4. A method for altering the ATP gradient across the biological membrane of a target bacteria, yeast, plant or mammalian cell to achieve a decrease in drug resistance comprising down-regulating an ecto-phosphatase in a target cell.

5. The method of claim 4 further comprising down-regulating an ABC transporter in a target cell.

6. A method for altering the ATP gradient across the biological membrane of a

plant cell to achieve an increase in drug resistance comprising up-regulating an ABC transporter in the target cell.

7. A method for altering the ATP gradient across the biological membrane of a plant cell to achieve a decrease in drug resistance comprising down-regulating an ABC transporter in the target cell.

8. A method for augmenting the chemotherapeutic effectiveness of a chemotherapeutic molecule by decreasing resistance to the chemotherapeutic molecule in a target cell comprising down-regulating an ecto-phosphatase in a target cell.

9. The method of claim 8 further comprising down-regulating an ABC transporter in the target cell.

10. A method for conferring herbicide resistance to a plant comprising up-regulating an ecto-phosphatase in the target cell.

11. The method of claim 10 further comprising up-regulating an ABC transporter in the target cell.

12. A method for increasing sensitivity to a drug molecule to inhibit or ameliorate

microorganism infection in animals and humans by altering the ATP gradient across the biological membrane of a microorganism to achieve a decrease in drug resistance comprising down-regulating an ecto-phosphatase in a target cell.

13. The method of claim 12 further comprising down-regulating an ABC transporter in a cell of the microorganism

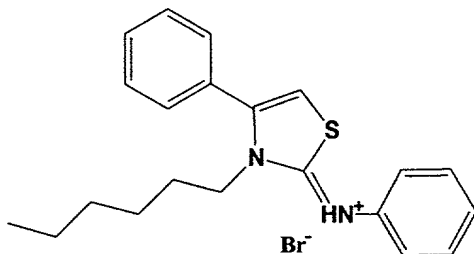
14. The method of claim 2, 4, 8, 10 or 12 wherein the ecto-phosphatase is selected from the group consisting of *Pisum sativum* apyrase (GenBank accession # Z32743) and *Homo sapiens* apyrases (GenBank accession # AF034840, AF039916, AF039917, AF039918 and HSU87967).

15. The method of claim 3, 5, 6, 7, 9, 11 or 13 wherein the ABC transporter is selected from the group consisting of *Arabidopsis thaliana* AtPGP-1 (GenBank accession # X61370), *Homo sapiens* Pgp (GenBank accession # M29432), *Homo sapiens* MDR- β (PCT publication WO 98/46736), *Saccharomyces cerevisiae* STS1 (GenBank accession # X75916), *Saccharomyces cerevisiae* Pdr5p (GenBank accession # 1420383), *Aspergillus fumigatus* Afu-MDR1 (U.S. Patent No. 5,705,352) and *Lactococcus lactis* LmrA (GenBank accession # U63741).

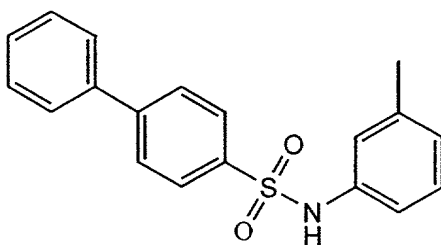
16. A method for inhibiting an ecto-phosphatase comprising contacting an ecto-

phosphatase with an ecto-phosphatase inhibiting amount of an ecto-phosphatase inhibitor

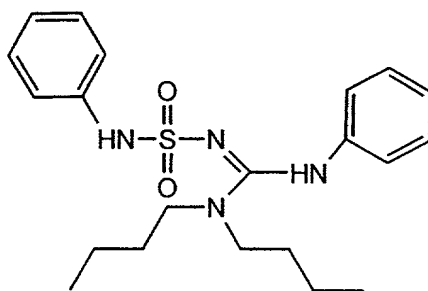
selected from the group consisting of molecules having the Formulae I through XIX:



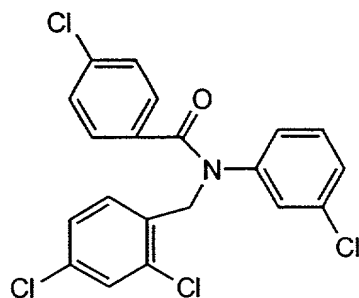
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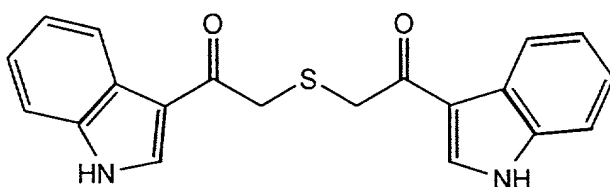
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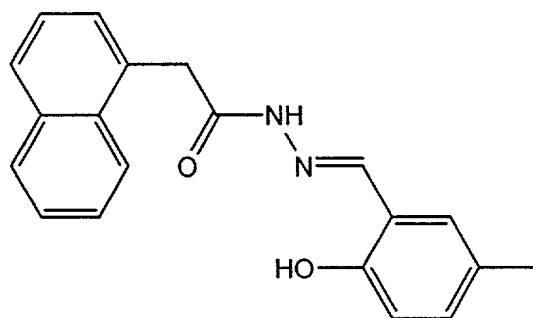
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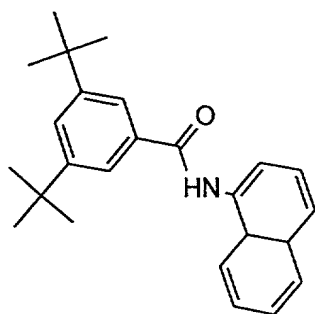


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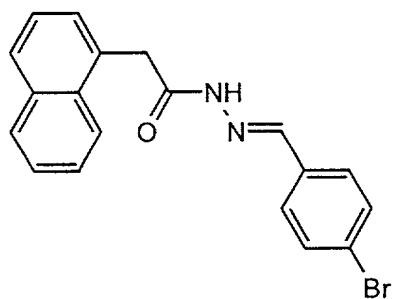


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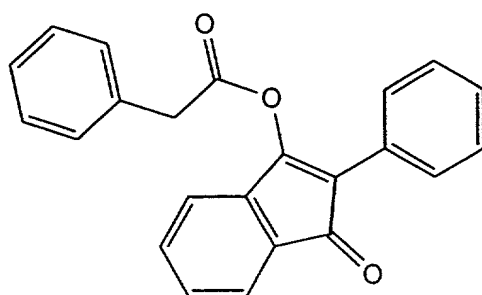
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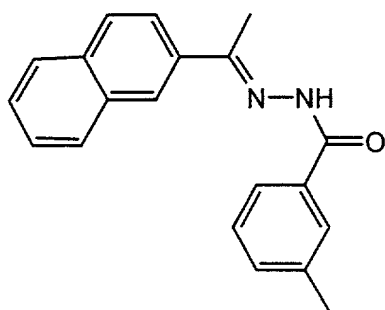


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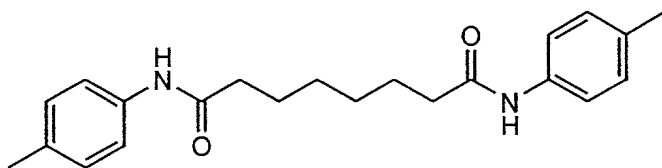


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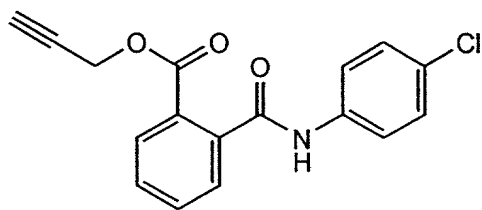
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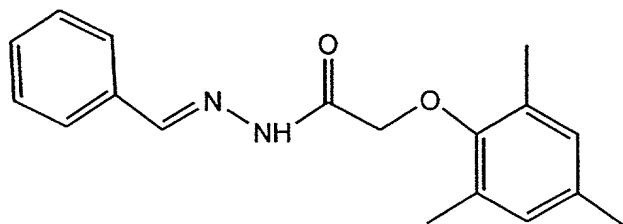
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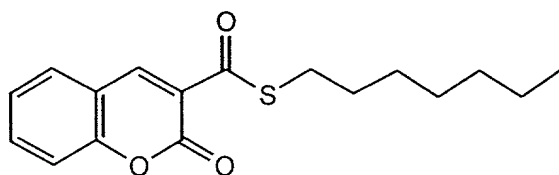
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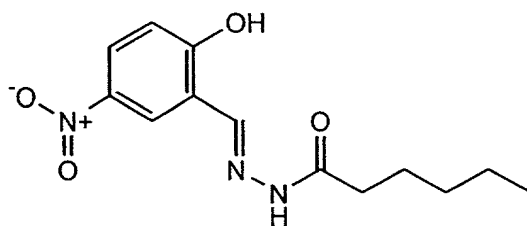
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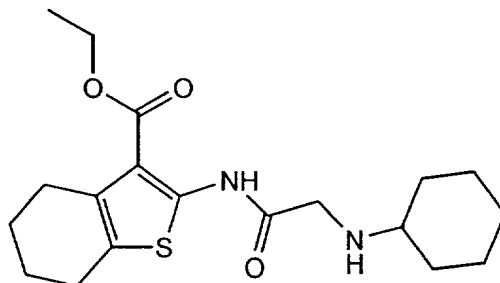
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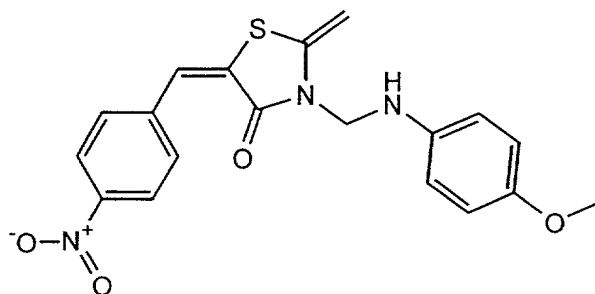
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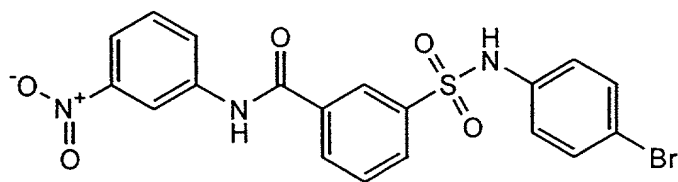
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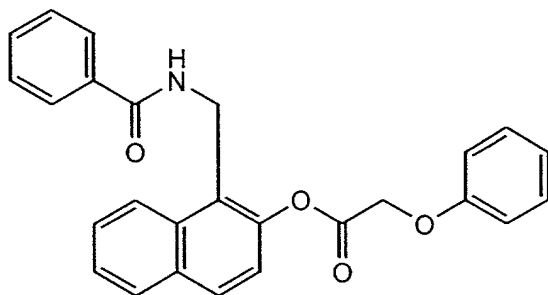
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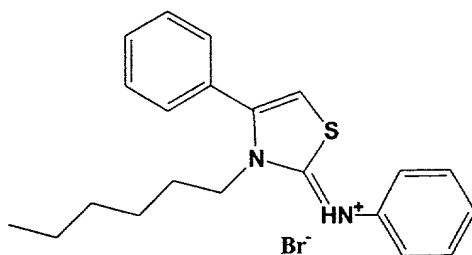
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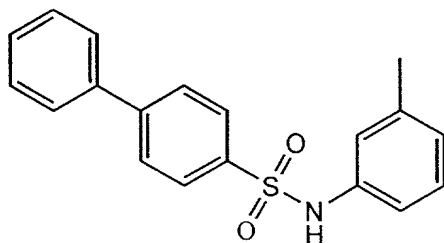
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17. The method of claim 16 wherein the ecto-phosphatase inhibitory molecule is selected from the group consisting of molecules having the Formulae I through V:

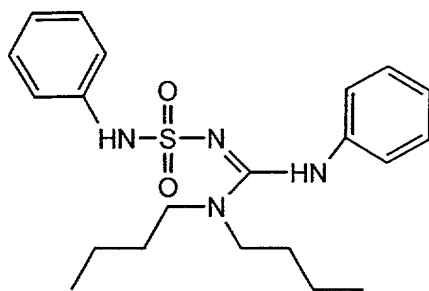
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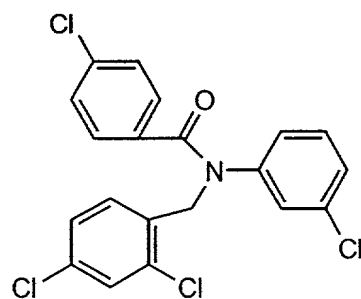


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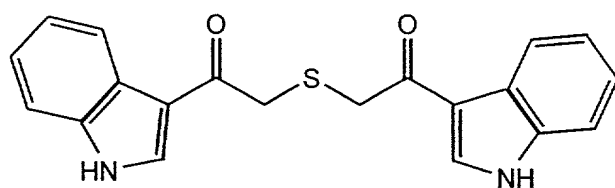


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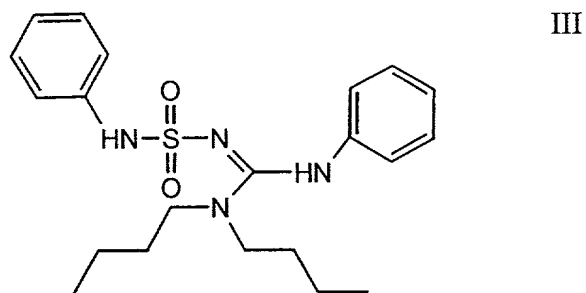
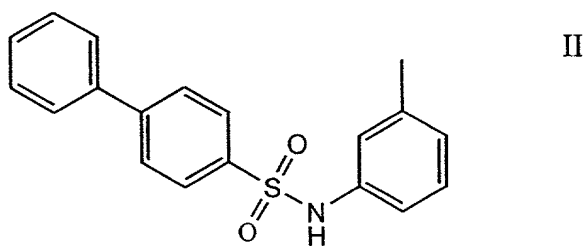
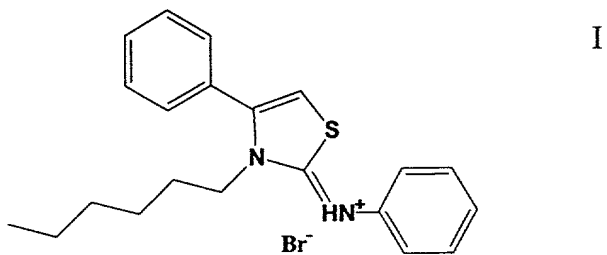


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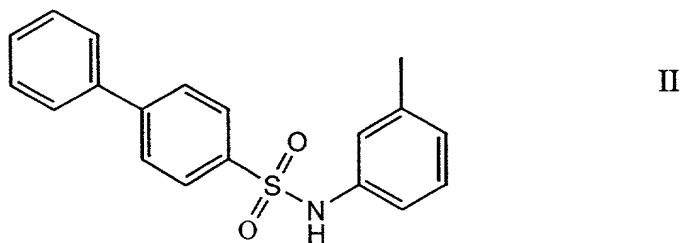
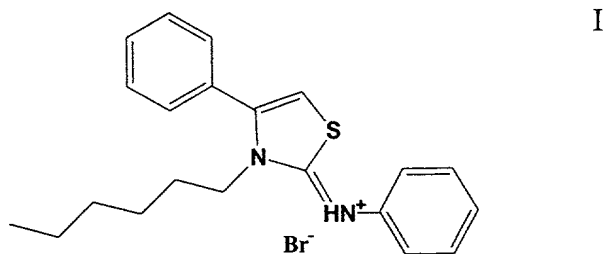
18. The method of claim 16 wherein the ecto-phosphatase inhibitory molecule is selected from the group consisting of molecules having the Formulae I through III:

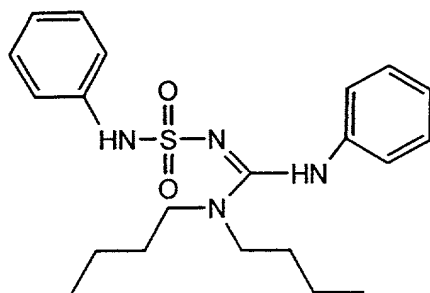


19. The method of claim 16 wherein the ecto-phosphatase is selected from the group consisting of *Pisum sativum* apyrase (GenBank accession # Z32743) and *Homo sapiens*

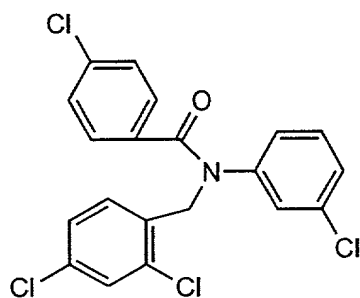
apyrases (GenBank accession # AF034840, AF0399ecto-phosphatase, AF039917, AF039918 and HSU87967).

20. A method for decreasing drug resistance in a target bacteria, yeast, plant or mammalian cell comprising introducing to cells a drug resistance-inhibiting amount of an ecto-phosphatase inhibitory molecule selected from the group consisting of molecules having the Formulae I through XIX:

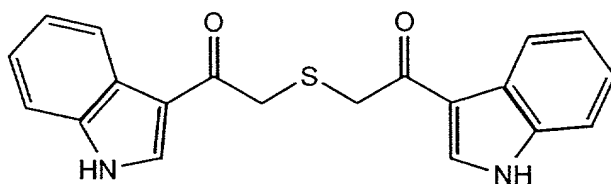




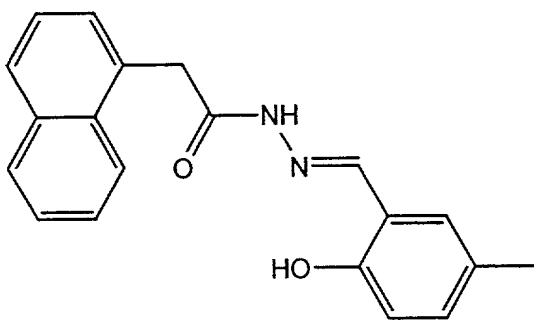
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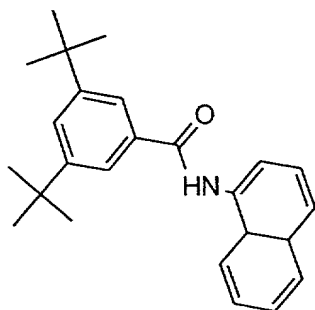
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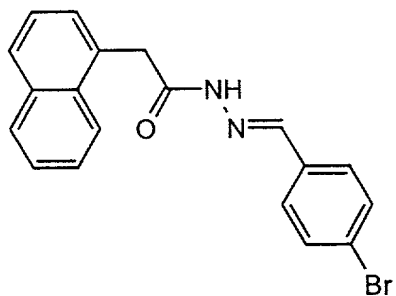
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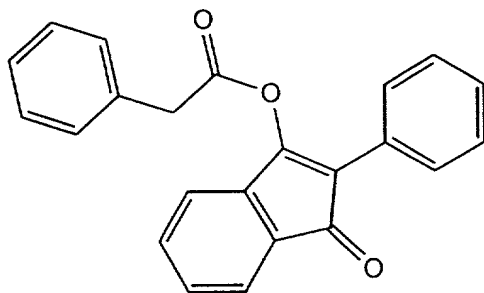
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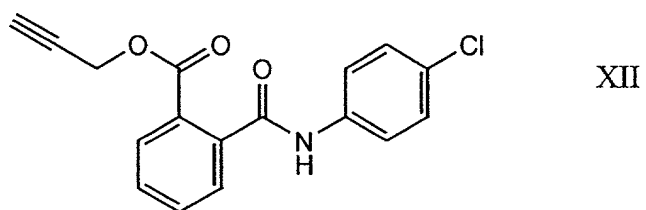
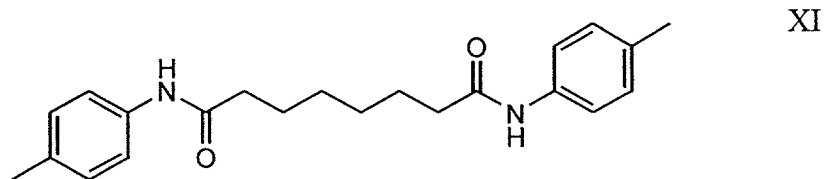
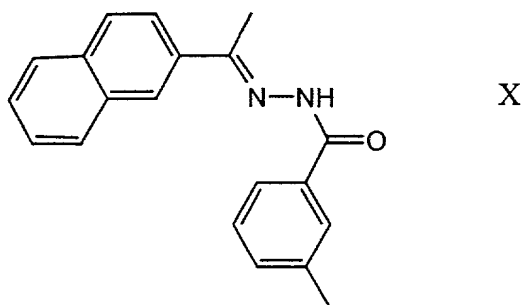
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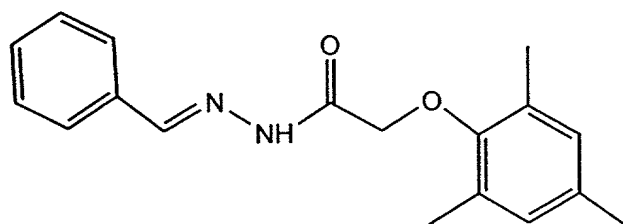


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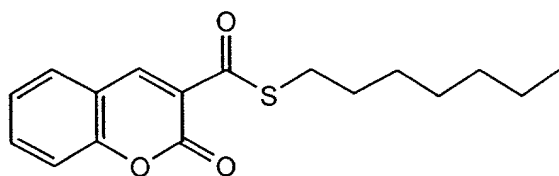


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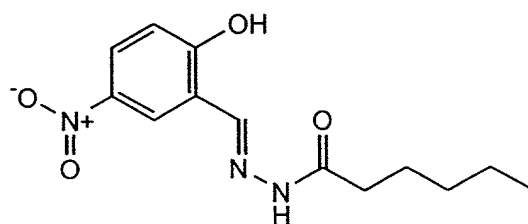




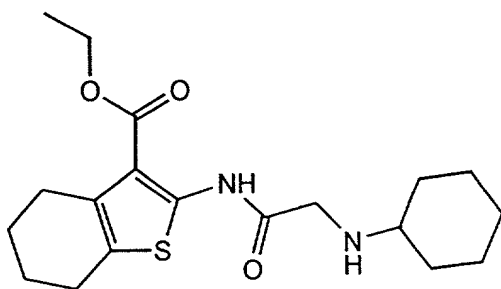
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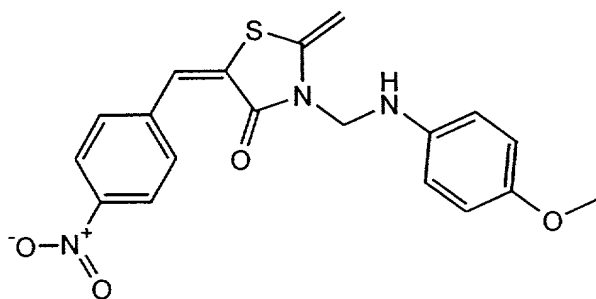
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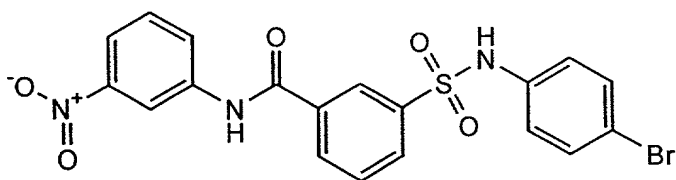
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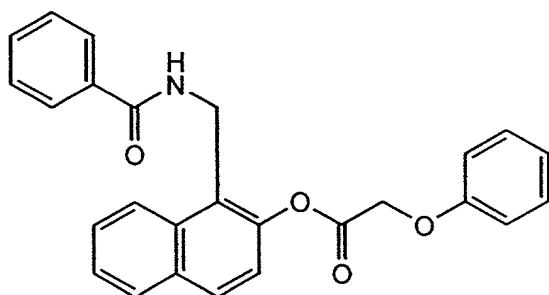
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XIX

21. The method according to claim 20 wherein the mammalian cells are tumor cells.
22. A method of identifying an inhibitor of an ecto-phosphatase comprising
 - a) contacting the ecto-phosphatase with a small molecule in the presence of ATP under conditions wherein the ecto-phosphatase has ATPase activity,
 - b) incubating the ecto-phosphatase, small molecule and ATP for a period of time sufficient to liberate phosphate from the ATP, and
 - c) adding ammonium molybdate and ascorbic acid to the ecto-phosphatase, small molecule and ATP to form a complex with liberated phosphate and to generate a dark blue color, wherein inhibition of the ecto-phosphatase by the small molecule results in less phosphate

liberated and less blue color.

23. The method according to claim 22 further comprising adding trisodium citrate and acetic acid.

24. The method according to claim 22 wherein the ecto-phosphatase is selected from the group consisting of *Pisum sativum* apyrase (GenBank accession # Z32743), *Homo sapiens* apyrase (GenBank accession # AF034840, AF0399ecto-phosphatase, AF039917, AF039918 and HSU87967) and potato apyrase (GenBank accession U58597).